

What is claimed is:

1. An empty sc-MHC class II molecule comprising a peptide binding groove and a class II  $\beta$ 2 chain comprising at least one amino acid substitution or deletion.
2. The empty sc-MHC class II molecule of claim 1 further comprising an immunoglobulin light chain constant region or fragment thereof.
3. An empty sc-MHC class II molecule comprising a peptide binding groove and covalently linked immunoglobulin light chain constant region or fragment.
4. A loaded sc-MHC molecule produced by contacting the empty sc-MHC class II molecule of claim 1, 2, or 3 with a presenting peptide under conditions which form a complex between the presenting peptide and the empty sc-MHC molecule.
5. A sc-MHC class II fusion protein comprising a recombinantly fused presenting peptide and a class II  $\beta$ 2 chain comprising at least one amino acid substitution or deletion.
6. The sc-MHC class II fusion protein of claim 5 further comprising an immunoglobulin light chain constant region or fragment thereof.
7. A sc-MHC class II fusion protein comprising a recombinantly fused presenting peptide and a covalently linked immunoglobulin light chain constant region or fragment.
8. An empty sc-MHC class II molecule comprising a peptide-binding groove, wherein the molecule comprises covalently linked in sequence:

- a) an MHC class II  $\beta 1$  chain or a presenting-peptide binding portion thereof,
- b) a class II  $\beta 2$  chain, comprising at least one amino acid substitution or deletion,
- c) a peptide linker sequence, and
- d) an MHC class II  $\alpha 1\alpha 2$  chain or a presenting-peptide binding portion thereof.

9. The empty sc-MHC class II molecule of claim 8, wherein the class II  $\beta 2$  chain amino acid deletion is essentially all of the class II  $\beta 2$  chain.

10. The empty sc-MHC class II molecule of claim 9 further comprising an immunoglobulin light chain constant region fragment covalently linked to the MHC class II  $\alpha 1\alpha 2$  chain or the presenting-peptide binding portion thereof.

11. An empty sc-MHC class II molecule comprising a peptide-binding groove, wherein the molecule comprises covalently linked in sequence:

- a) an MHC class II  $\beta 1 \beta 2$  chain or a presenting-peptide binding portion thereof,
- b) a peptide linker sequence,
- c) an MHC class II  $\alpha 1\alpha 2$  chain or a presenting-peptide binding portion thereof, and
- d) an immunoglobulin light chain constant region fragment.

12. The empty sc-MHC class II molecule of claim 11, wherein the immunoglobulin light chain constant region fragment is a murine or human C $\kappa$  chain.

13. The empty sc-MHC class II molecule of claim 11, wherein the immunoglobulin light chain constant region fragment is a murine or human C $\lambda$  chain.

14. A loaded sc-MHC molecule produced by contacting the empty sc-MHC class II molecule of claims 8 or 11 with a presenting peptide under conditions which form a complex between the presenting peptide and the empty sc-MHC class II molecule.

~~15.~~ A sc-MHC class II fusion molecule comprising a peptide-binding groove, the sc-MHC class II fusion molecule comprising covalently linked in sequence:

- a) a presenting peptide,
- b) an MHC class II  $\beta 1$  chain or a presenting-peptide binding portion thereof,
- c) an MHC class II  $\beta 2$  chain comprising at least one amino acid substitution or deletion
- d) a peptide linker sequence; and
- e) an MHC class II  $\alpha 1 \alpha 2$  chain or a presenting-peptide binding portion thereof.

16. The sc-MHC class II fusion molecule of claim 15, wherein the class II  $\beta 2$  chain deletion comprises deletion of at least 2, 5, 10, 25, 50, 60, 70, 80, 90 or greater amino acids of the class II  $\beta 2$  chain.

17. The sc-MHC class II fusion molecule of claim 16, wherein the class II  $\beta 2$  chain amino acid deletion is essentially all of the class II  $\beta 2$  chain.

18. The sc-MHC class II fusion molecule of claim 15, wherein the class II  $\beta 2$  chain substituted comprises a substitution of 2, 5, 10, 25, 50, 60, 70, 80, 90 or greater amino acids of the class II  $\beta 2$  chain.

19. The sc-MHC class II fusion molecule of claim 18, wherein the class II  $\beta 2$  chain substitution comprises a Cys<sup>117</sup> to Ser<sup>117</sup> substitution.

20. The sc-MHC class II fusion molecule of claim 15 further comprising an immunoglobulin light chain constant region fragment covalently linked to the MHC class II  $\alpha 1 \alpha 2$  chain or the presenting-peptide binding portion thereof.

21. A sc-MHC class II fusion molecule comprising a peptide-binding groove, wherein the fusion molecule comprises covalently linked in sequence:

- a) a presenting peptide,
- b) an MHC class II  $\beta 1 \beta 2$  chain or a presenting-peptide binding portion thereof,
- c) a peptide linker sequence,
- d) an MHC class II  $\alpha 1 \alpha 2$  chain or a presenting-peptide binding portion thereof, and
- e) an immunoglobulin light chain constant region (Ig-C<sub>L</sub>) or fragment.

22. The sc-MHC class II fusion molecule of claim 21, wherein the immunoglobulin light chain constant region fragment is a murine or human C $\kappa$  chain.

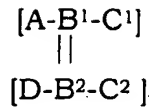
23. The empty sc-MHC class II molecule of claim 21, wherein the immunoglobulin light chain constant region fragment is a murine or human C $\lambda$  chain.

24. The sc-MHC class II fusion molecule of claim 22 or 23 wherein the immunoglobulin light chain constant region (Ig-C<sub>L</sub>) fragment is between about 80 to 130, 90 to 120, or 100 to 110 amino acids in length.

25. An empty polyspecific MHC complex comprising an sc-MHC class following general formula:

1122nd

Sub  
43



wherein,

*Sub  
a3*

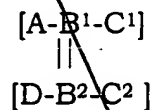
- a) A represents at least one empty sc-MHC class II molecule, <sup>112</sup>
- b) B<sub>1</sub>, B<sub>2</sub> are each independently a joining molecule, <sup>which are</sup> the same or different,
- c) C<sub>1</sub>, C<sub>2</sub> are each independently an effector molecule, <sup>which are</sup> the same or different or -H; and
- d) D represents at least one empty sc-MHC class II molecule, ligand binding molecule or -H.

26. A polyspecific MHC complex comprising an empty sc-MHC class II molecule comprising a peptide binding groove, the complex being represented by the formulae A-B-C, B-A-C, or A-C-B, wherein A is at least one sc-MHC class II molecule, B is a joining molecule and C is an effector molecule or -H, provided that when the complex is represented by A-C-B, -C- is not -H.

27. A loaded polyspecific MHC complex formed by contacting the polyspecific MHC complexes of claim 25 or 26 with a presenting peptide under conditions which form a specific binding complex between the presenting peptide and at least one of the empty sc-MHC class II molecules.

28. A polyspecific MHC complex fusion molecule comprising an sc-MHC molecule with peptide binding groove, the complex being represented by the following formula:

*Sub  
A4*



wherein,

*not  
2.24.9*

a) A represents at least one sc-MHC class II molecule comprising a recombinantly fused presenting peptide, *which are*

b) B<sub>1</sub>, B<sub>2</sub> are each independently a joining molecule, *the same or different,*

c) C<sub>1</sub>, C<sub>2</sub> are each independently an effector molecule, *the same or different or -H<sub>2</sub> and*

d) D represents at least one, sc-MHC class II molecule comprising a recombinantly fused presenting peptide, ligand binding molecule or -H.

29. A polyspecific MHC fusion molecule comprising a sc-MHC class II molecule comprising a peptide binding groove, the complex being represented by the formulae: A-B-C, B-A-C, or A-C-B, wherein A is at least one sc-MHC class II molecule comprising a recombinantly fused presenting peptide, B is a joining molecule and C is an effector molecule or -H, provided that when the complex is represented by the formulae: A-C-B, -C- is not H.

30. A DNA segment encoding the sc-MHC class II molecule of claim 1, 3, 5, or 7.

31. A DNA segment encoding at least a portion of the polyspecific MHC molecule of claim 22 and 26.

32. A DNA vector comprising the DNA segments of claim 27.

33. A DNA vector comprising the DNA segments of claim 29.

34. A method of manufacturing a sc-MHC class II molecule comprising a  $\beta 2$  class II chain modification, the method comprising:

a) providing a cell comprising a DNA vector, wherein the DNA vector comprises DNA sequence encoding the sc-MHC class II molecule comprising the  $\beta 2$  class II chain modification,

Sub  
A4

- b) culturing the cell in medium under conditions which permit expression of the sc-MHC class II molecule; and
- c) purifying the sc-MHC class II molecule from the cell or medium.

35. The method of claim 34, wherein the sc-MHC class II molecule comprising the  $\beta 2$  class II chain modification is the sc-MHC class II molecule recited in claim 1, 3, 5 or 7.

36. A method of manufacturing a polyspecific MHC class II complex, the method comprising:

- a) providing a cell comprising one or more DNA vectors, which vectors comprise a DNA sequence encoding the polyspecific MHC complex or a portion thereof capable of specifically binding a joining molecule,
- b) culturing the cell in medium under conditions which permit expression of the polyspecific MHC molecule; and
- c) purifying the polyspecific MHC molecule from the cell or medium.

37. A method of suppressing an immune response in a mammal comprising administering to the mammal an effective amount of the sc-MHC complex of claim 4, 5, 7, 17 or 28.

add  
a5

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